Minocycline for Treatment of Posttraumatic Stress Disorder in Veterans: A Case Series

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Abstract

PTSD is a major public health problem associated with significant disability, suboptimal treatment response and relapses. We report a case series of veterans with PTSD successfully treated with adjunctive minocycline. Studies have shown that chronic stress associated with PTSD may be related to chronic inflammation, observed through increased levels of pro-inflammatory markers. Minocycline is a broad-spectrum tetracycline antibiotic with anti-inflammatory and neuroprotective properties. In an animal model of PTSD, decreased cytokine levels were found in those treated with minocycline compared to controls. We reviewed medical records of patients who participated in a 12-week study evaluating the efficacy of minocycline in treating PTSD. All patients decreased their Clinician-Administered PTSD Scale for DSM-5 scores (CAPS-5) by the end of the study. C-reactive protein levels decreased or remained the same, and the results of other inflammatory markers such as IL-6 and TNF-α warrant further exploration. Adjunctive minocycline was not associated with any serious adverse events or laboratory abnormalities. With no data yet published on the efficacy of minocycline treatment in veterans with PTSD, these findings could be expanded on in a larger clinical trial.

Background

Posttraumatic stress disorder (PTSD) is a debilitating disorder characterized by re-experiencing an original trauma, avoidance of trauma reminders, and hyperarousal. The prevalence of PTSD in the community is around 6.8%, and in veterans it is higher: 12.5% for Operation Enduring Freedom veterans and 30% for Operation Iraqi Freedom veterans.[1,2] Cumulative stress has been suggested to play an important role in PTSD development. For example, studies suggest the risk for developing PTSD is greater in military units with longer deployments.[3] Chronic inflammation, observed through levels of pro-inflammatory markers, has also been implicated in disease development.[4] Increased CRP levels have been associated with depression and PTSD symptoms in active military personnel, and veterans with PTSD have been shown to exhibit higher levels of pro-inflammatory markers than veterans without PTSD. [4,5] PTSD has been linked to an increased risk of diseases such as cardiovascular and autoimmune disease, which both have an inflammatory aspect.[6]

The above studies suggest that the inflammatory response may be a potential drug target for PTSD. Minocycline is a broad-spectrum tetracycline antibiotic that also exhibits neuroprotective and anti-inflammatory actions. In an animal model, decreased inflammatory cytokine levels were associated with minocycline.[7] A recent study of fear conditioning in humans using doxycycline, another tetracycline antibiotic, suggested this drug class may be helpful in improving symptoms of PTSD.[8] 20 Despite these findings, there is no published data on efficacy of minocycline treatment in veterans with PTSD.

Methods

Participants:

Four patients who previously participated in 12-week open label pilot study at Nebraska-Western Iowa Health Care System to evaluate efficacy of minocycline in treating PTSD.

All patients were instructed to take 100 mg/day of adjunctive minocycline for 7 days, followed by 200mg/day for the remainder of the study.

Inclusion Criteria:

1. Veterans between ages 19-65 who met DSM-5 criteria for chronic PTSD
2. Adequate, stable dose of psychotropic med for minimum of 8 weeks at time of study entry
3. Allowed to have other comorbid symptoms common with PTSD such as anxiety or somatic symptoms

Exclusion Criteria:

1. Concurrent DSM-5 diagnosis of:
   Major Neurocognitive Disorder, Lifetime Schizophrenia and other Psychotic Disorders, Lifetime Bipolar Disorder, Alcohol Dependence or Abuse in 3 months prior to screening, Substance Dependence or Abuse (excluding nicotine) in 12 months prior to Screening Visit.
2. Statin use (shown to reduce levels of pro-inflammatory cytokines)
3. Concomitant treatment with penicillin or other antibiotics, or treatment with antibiotics greater than 7 days in the past month.

Procedure

The following clinical measures were used for assessment:

- Mini-International Neuropsychiatric Interview (MINI) – screening tool for comorbid psychiatric disorders
- PTSD Checklist for DSM-5 (PCL-5) – used to confirm PTSD diagnosis
- Beck Depression Inventory (BDI-II) – used to assess depression symptoms
- Clinician Administered PTSD Scale for DSM-5 (CAPS-5) – used to assess current (past month) PTSD symptoms
- Clinical Global Impressions (CGI) scale – displays overall severity and improvement of symptoms

Pro-inflammatory cytokines measured:

- C reactive protein
- IL-6
- TNF- α

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Results

	Change in CAPS Score	Change in BDI-II Score	Change in CRP Levels (mg/dL)	Change in IL-6 Levels (pg/dL)	Change in TNF-α levels (pg/dL)
Patient A	Decreased by 8	Decreased by 5	Remained below 0.5	Increased by 0.21	Decreased by 0.26
Patient B	Decreased by 11	Increased by 12	Decreased by 0.50	Decreased by 0.30	Decreased by 0.21
Patient C	Decreased by 11	Decreased by 6	Decreased by 0.20	Increased by 0.77	Increased by 0.29
Patient D	Decreased by 4	Decreased by 16	Remained below 0.5	Increased by 0.81	Increased by 0.15

Conclusions

- All four patients had decreased CAPS scores by the end of the study.
- CRP levels decreased or remained below 0.5 mg/dL in all patients
- It was expected that elevations in CRP would mirror elevations of IL-6 and TNF- α, however three subjects had increased IL-6 levels, and two subjects had increased TNF- α levels.
  - CRP has a longer half-life than IL-6 or TNF- α, and rise in IL-6 and TNF-α without CRP could be attributed to acute phase responses in patients with differing subclinical inflammation[9]
- Limitations included the study included the lack of a placebo arm, short trial length, and lack of follow-up to assess long-term benefits.
- Adjunctive minocycline has already been shown to improve depression symptoms,[10] and patients A, C, and D had decreased BDI-II scores by a notable margin during the study.
- Further research with large double-blind clinical trials should be considered for this inexpensive and generally safe drug in treating PTSD and adjunctive symptoms.

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